REMARKS/ARGUMENTS

Claims 11-15, 20-25, 32-37 and 39-73 remain pending in this application. Claims 1-38 are cancelled without prejudice. Claims 39 and 57 are amended herewith. Claims 39-47 and 52-73 are rejected under 35 U.S.C. § 103(a). It is noted that the Examiner issued a new ground of rejection in view of Armitage and Gruber. *See* page 2, Office Action. However, no specific reference to Gruber is made in the obviousness rejections under §103(a). Therefore, Applicant will respond to the obviousness rejections in view of Armitage and Arvanitidou as discussed throughout the Office Action, rather than Gruber. In view of this discrepancy, Applicant respectfully requests that the finality of the present Office Action be withdrawn. Reconsideration of the application in view of the amendments and remarks set forth below is respectfully requested.

Claim Rejections Under 35 U.S.C. §103

Claims 39-47 and 52-73 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Armitage *et al.* (WO 9220334) in view of Arvanitidou *et al.* (WO 96/19982) because it would have been obvious to one or ordinary skill in the art to optimize the compression force and crushing strength by routine experimentation to formulate a therapeutically feasible composition. Applicant traverses this rejection. The rejection is traversed on the grounds that the Examiner has not set forth a *prima facie* case of obviousness. As explained in the MPEP:

> [t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP § 2143.

Notably, the Examiner fails to discuss how the claims are unpatentable in view of Arvanitidou or in view of the combination of Armitage and Arvanitidou. More importantly, nowhere does the Examiner point to a suggestion to combine Armitage and Arvanitidou. The Examiner cites Armitage for teaching solid compositions comprising sodium salts of racemic ibuprofen and sodium carbonate in the form of granules. The present invention provides an improved non-effervescent compressed dosage form which permits delivery of high therapeutic levels of the sodium salt of racemic ibuprofen to the gastrointestinal tract of a patient.

The specification at page 7, line 21 indicates that the sodium salt of racemic ibuprofen is a flaky, soft and sticky material. Consequently, it does not lend itself to formulation into a directly compressed dosage form as it typically sticks to the tableting punches. Moreover, it is also difficult to pre-granulate the sodium salt of racemic ibuprofen prior to compression with other excipients. Suitably, in order to form satisfactory compressed dosage forms of the sodium salt of racemic ibuprofen, it is necessary to pre-treat the salt (*e.g.*, milling). It is well recognized in the art that the sodium salt of racemic ibuprofen is a hygroscopic tacky and flaky material that is difficult to compress into tablets. It would not have been obvious to one of ordinary skill in the art at the time of the invention to optimize the compression force and crushing strength by routine experimentation.

Unexpectedly, if sodium carbonate is mixed with the sodium salt of racemic ibuprofen, then the resulting mixture exhibits improved flowability and compressibility. The mixture may be compressed directly into tablets as it does not stick to the punches of the tableting machine. Consequently, the addition of sodium carbonate to the sodium salt of racemic ibuprofen overcomes the known problems in the art associated with compressing the sodium salt of racemic ibuprofen. Conveniently, it is not necessary to pre-treat the sodium salt of racemic ibuprofen prior to compression and the sodium salt may be taken directly from a bulk production process. *See* specification at page 7, lines 21-31.

The inclusion of sodium carbonate also enhances the compressibility of the pharmaceutical composition comprising a compressible filler and disintegrant. Suitably, the

composition used to form the compressed dosage form may be compressed by applying the compression forces of standard tableting machines to produce a compressed dosage form which exhibits improved hardness so that it does not break up during further manufacturing steps. In addition, the composition maintains an acceptable relatively fast disintegration time to permit an on-set hastened therapeutic action compared with a composition not including sodium carbonate. *See* specification at page 2, lines 1-20 and page 3, lines 8-14. This is clearly demonstrated by the results of Tables 1 and 2 and page 31 of the specification.

Claims 39-47 and 52-73 are rejected as unpatentable over Armitage *et al.* in view of Arvanitidou (WO 96/19982) because the Examiner argues that it would have been obvious to eliminate malic acid in Armitage and formulate a non-effervescent solid dosage formulation as shown by Arvanitidou. Applicant respectfully traverses the rejection in view of the following comments.

As an initial matter, Armitage and Arvanitidou fail to teach or suggest all the elements of the rejected claims. "When a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references." *In re Rouffet*, 47 USPQ2d 1453, 1456 (Fed. Cir. 1998); *see also* MPEP § 2143.01. Virtually all inventions are combinations of old elements. *See In re Rouffet*, 47 USPQ2d at 1457. If identification of each claimed element in the prior art were sufficient to negate patentability, the Examiner could use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. *Id.* To prevent the use of hindsight based on the teachings of the patent application, the Examiner must show a motivation to combine the references in the manner suggested. *Id. at 1457-1458.*

In *Rouffet*, the Court of Appeals held that the Board of Patent Appeals and Interferences did not err in finding that all elements recited in the claims of Rouffet's application were contained in the combined disclosures of three prior art references. *See In re Rouffet*, 47 USPQ2d at 1457. The Court did hold, however, that the Board erred in determining that one skilled in the art would have been motivated to combine the references in such a manner as to render the

claims obvious. *Id. at 1457.* The situation is, at best, the same in this case. Even if all elements recited in the claims can be found in the combined disclosures of Armitage and Arvanitidou, there is no reason that one of ordinary skill in the art would have been motivated to combine these references in such a manner as to render the claims obvious.

The claims are broadly directed to a solid non-effervescent coated compressed dosage form comprising a racemic ibuprofen medicament in the form of the sodium salt and sodium carbonate. Neither Armitage nor Arvantidou describe granules used as a non-effervescent formulation. The Examiner acknowledges this fact, but pulls elements from both Armitage and Arvanitidou to arrive at the claimed invention. It is inappropriate to simply "pick and choose among the individual elements of assorted prior art references to recreate the claimed invention." *SmithKline Diagnostics, Inc. v. Helena Laboratories Corp.*, 859 F.2d 878, 887 (Fed. Cir. 1988). The Examiner must show that the prior art as a whole would have suggested the claimed invention to one of ordinary skill in the art.

There is no reason why one skilled in the art reading Armitage and Arvanitidou would combine sodium carbonate with the sodium salt of racemic ibuprofen with the expectation of improving the flowability and compressibility of the sodium salt of racemic ibuprofen in order to arrive at a compressed non-effervescent tablet as claimed. In fact, Armitage actively teaches away from such a compressed tablet. Rather, Armitage solves a different technical problem than the one solved by the present invention.

Armitage relates to producing a specific enantiomer of ibuprofen, namely S(+)-ibuprofen, the sodium salt of S-(+)-ibuprofen and pharmaceutical compositions containing such compounds. In particular, Armitage relates to overcoming the problems of formulating S(+)-ibuprofen as it typically exhibits poor flow characteristics. This is achieved by using the sodium salt of a specific flowability. *See* col. 1, lines 7-24, lines 35-40 and line 63 to col. 2, line 6. Armitage is not concerned with improving the flowability and compressibility of the sodium salt of racemic ibuprofen. This may be achieved in the present invention by adding sodium carbonate to sodium salt. Specific enantiomers of a particular compound exhibit different physical and chemical than

the racemic mixture.

Armitage is directed solely to the sodium salt of a specific enantiomer of ibuprofen, as it is this specific enantiomer which is the active agent in racemic ibuprofen. Armitage is not concerned with compositions which include racemic ibuprofen. See col. 1, lines 17-22. Thus, one skilled in the art would not replace the sodium salt of S-(+)-ibuprofen in any of the formulations disclosed in Armitage, because this is completely contrary to the teaching of Armitage. Moreover, as mentioned previously, it is well recognized in the art that the sodium salt of racemic ibuprofen exhibits poor flow and compressibility characteristics as disclosed in DE 3922441 which is identified at col. 1, lines 25-35 of Armitage.

The examiner refers to Example 18 of Armitage and asserts that the effervescent granules include all of the features of the claimed non-effervescent compressed tablet when read in conjunction with the general description of Armitage and Arvanitidou. Applicant respectfully disagrees. In particular, the effervescent granules of Example 18 include the sodium salt of a specific enantiomer of ibuprofen (*i.e.*, S(-)sodium 2-(4-isobutylphenylproprionate), and not the sodium salt of racemic ibuprofen. Thus, even if one skilled in the art were motivated to remove the malic acid from the formulation of Example 18 and compress the resulting composition to form a non-effervescent compressed tablet as suggested by the examiner, then such a compressed tablet would not fall within the scope of the invention as claimed because it would include S-(-)sodium ibuprofen and not the sodium salt of racemic ibuprofen. A skilled person, in order to arrive at the non-effervescent compressed tablet as claimed in the present invention, must take the non-obvious step of replacing S-(-)sodium ibuprofen with the sodium salt of racemic ibuprofen. As discussed above, Armitage actively teaches away from such a replacement as it is concerned with improving the processability of the active enantiomer of ibuprofen and to make such a replacement is completely contrary to the teachings of Armitage.

Arvanitidou fails to make up for the deficiencies in Armitage. Arvanitidou is concerned with improving the water solubility of ibuprofen free acid. *See* page 3, penultimate paragraph. This is achieved by admixing ibuprofen free acid with an inorganic alkaline salt (page 4).

Arvanitidou is not concerned with ibuprofen salts, let alone the sodium salt of racemic ibuprofen. Consequently, Arvanitidou does not teach or suggest that the problems associated with processing the sodium salt of racemic ibuprofen be improved by mixing it with sodium carbonate. Therefore, the claims are not obvious in view of Armitage and Arvanitidou. Applicant respectfully requests that the rejection on this basis be withdrawn.

In view of the above amendments and remarks, Applicant submits that the present application is now in condition for allowance. Reconsideration and favorable action are requested. The Examiner is invited to telephone the undersigned to expedite allowance of this application.

RESPECTFULLY SUBMITTED,					
NAME AND REG. NUMBER	Leigh Z. Callander, Registration No. 55,035				
SIGNATURE			DATE	April 26, 2006	
ADDRESS	Rothwell, Figg, Ernst & Manbeck 1425 K Street, N.W., Suite 800				
CITY	Washington	*State*	D.C.	*Zip Code*	20005
COUNTRY	U.S.A.	*Telephone*	202-783-6040	*Fax*	202-783-6031

2955-101.am6.wpd